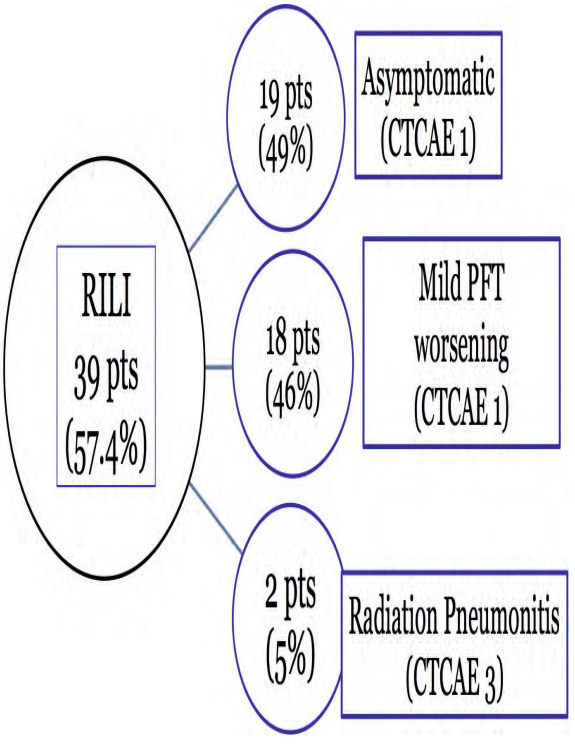
PO-0679

Radiation-induced lung injury (RILI): correlation with dosimetric parameters and pulmonary function

G.R. D'Agostino[1], F. De Rose[1], M. Balducci[1], F. Micciché[1], A.R. Larici[1], S.I. Santoro[1], A. Castelluccia[1], G.M. Corbo[2], V. Valentini[1], G. Mantini[1]
[1]*Università Cattolica del Sacro Cuore, Radiology and Radiotherapy, Rome, Italy*
[2]*Università Cattolica del Sacro Cuore, Pneumology, Rome, Italy*

Purpose/Objective: Radiation-induced lung injury (RILI) is the most common side effect after radiation therapy for lung cancer. It is well known that the radiological finding of RILI is not always associated with the clinical manifestation of pneumonitis, and it is also not clear if it correlates with a decrease of patient's pulmonary function. In this study, we analyzed the predictive value of dosimetric parameters and Pulmonary Function Tests (PFTs), and their correlation with the radiological incidence of radiation-induced lung injury (RILI).
Materials and Methods: Data from patients with non-small cell lung cancer (NSCLC), stage I-IIIB, treated with (chemo)-radiation in our Institution were analyzed. Eligibility criteria were: presence of visible tumor on a diagnostic chest CT scan, availability of CT scans before irradiation and at 3-6 months follow-up, baseline PFTs, with at least forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), total lung capacity (TLC), functional residual capacity (FRC) and vital capacity (VC) at 2-4 months follow-up.
Results: Data from 68 patients treated from 2005 to 2012 were analyzed. The worsening of pulmonary function was evaluated comparing PFTs performed before and after radiotherapy. We tested the difference of percentage of predicted value of all the parameters and we obtained statistically significant results for Functional Residual Capacity (FRC), Total Lung Capacity (TLC), Vital Capacity (VC) and Functional Vital Capacity (FVC). Thirty-nine patients (57,4%) developed radiation-induced changes in lung tissue. Eighteen patients (26.6%) experienced a radiologically defined RILI associated to a worsening of respiratory performance. Nevertheless, these patients did not show the signs and symptoms of radiation pneumonitis, nor did their respiratory impairment interfere with the activities of daily living. The remaining 19 patients (28.0%) had a post-treatment radiological diagnosis of RILI without any respiratory impairment during and/or post treatment. Two patients showed clinical signs of pneumonitis with only one of them experiencing a worsening of PFTs. Logistic regression was performed to verify whether the commonly used lung dosimetric constraints could be predictive of RILI. MLD was found to be the strongest predictor of RILI (Odds Ratio:1.19; 95% CI: 1.04 – 1.35; p: 0.009), but even V20, V30, V5, ipsilateral V20 proved to be significantly related to the onset of RILI.



Conclusions: Our study confirmed the important role of dosimetric parameters for the prediction of lung toxicity. It also proved that the radiological finding of RILI does not necessarily correlate with a worsening of the patient's respiratory performance, especially when treatment planning has been performed complying with the lung dosimetric constraints.

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Diagnostic delay is an independent prognostic factor in patients treated for stage I-III small cell lung cancer

B. Reymen[1], J. van Loon[1], A. van Baardwijk[1], R. Wanders[1], E. Troost[1], F. Hoebers[1], D. De Ruysscher[2], P. Lambin[1]
[1]*MAASTRO Clinic, Dpt. of Radiotherapy, Maastricht, The Netherlands*
[2]*UZ Leuven, Dpt. of Radiotherapy, Leuven, Belgium*

Purpose/Objective: Because small-cell lung cancer has a short doubling time, clinicians strive to obtain a diagnosis as soon as possible. We investigated the value of a short diagnostic process in a prospectively collected cohort of SCLC patients.
Materials and Methods: Analysis of patients in our prospective database with stage I-III SCLC referred for concurrent chemo-radiotherapy. Standard treatment was 45 Gy in 1.5 Gy fractions twice daily concurrently with carboplatin-etoposide, followed by prophylactic cranial irradiation (PCI) in case of non-progression. Survival was calculated from pathologic diagnosis (Kaplan-Meier method). Diagnostic delay was defined as the time between the first report of suspicious findings on imaging and the date of pathological verification of SCLC status.
Results: 73 patients were included in the present analysis. Median overall survival was 20 months (95% CI 17.8-22.2 months), 2-year survival 38%. Median time between first imaging and pathology was 19±64 days (range -1-505 days). Median time between pathology and start of chemotherapy was 13±10 days (range 0-47 days). In multivariate Cox regression analysis including WHO-PS, age, gender, LDH, PCI, SER, Gross Tumor Volume (GTV) and stage only the diagnostic delay significantly impacted overall survival (p=0.018). The hazard ratio for death per week delay was 1.04, amounting to a hazard ratio of 1.18 per month (28 days) delay. The time between pathology date and start of chemotherapy did not significantly impact overall survival in this cohort.
Conclusions: In this series of stage I-III small cell lung cancer treated with concurrent chemo-radiation, diagnostic delay is an independent risk factor for stage I-III SCLC.

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Histology-specific glucose metabolism and the tumor microenvironment in NSCLC

J. Bussink[1], T.W.H. Meijer[1], O.C.J. Schuurbiers[2], L.F. de Geus-Oei[3], P.N. Span[1], J.H.A.M. Kaanders[1]
[1]*Radboud University Nijmegen Medical Center, Radiation Oncology, Nijmegen, The Netherlands*
[2]*Radboud University Nijmegen Medical Center, Pulmonary Diseases, Nijmegen, The Netherlands*
[3]*Radboud University Nijmegen Medical Center, Nuclear Medicine, Nijmegen, The Netherlands*

Purpose/Objective: Tumor behavior and treatment outcome of subgroups of non-small cell lung carcinoma (NSCLC) patients mainly depend on histology. In the present study, differences in glucose metabolism between adeno- and squamous cell NSCLCs were quantified using the hypoxia and glycolysis-related markers GLUT1, CAIX, MCT1, MCT4, vascular density, as well as ^{18}FDG-PET imaging in curatively resected NSCLC patients. The relevance of these metabolic markers for disease-free survival (DFS) were analyzed.
Materials and Methods: In 111 patients, pre-treatment ^{18}FDG-uptake was quantified by calculating SUVmax and TLGmax. Metabolic marker expression, measured by immunofluorescent staining (protein) and qPCR (mRNA), and vascular density were determined in 90 fresh frozen resection specimens. Patients were retrospectively evaluated for DFS.
Results: mRNA and protein expression of metabolic markers, with the exception of MCT4, and ^{18}FDG-uptake were higher in squamous cell carcinomas than in adenocarcinomas, whereas adenocarcinomas were better vascularized. Adenocarcinomas had a worse DFS compared to squamous cell carcinomas (p=0.016) based on the potential to metastasize. High glucose consumption, as assessed by GLUT1 mRNA, SUVmax or TLGmax, was associated with a worse DFS in only adenocarcinomas.
Conclusions: Our findings indicate that adenocarcinomas exhibit glycolysis under normoxic conditions close to the vessels, whereas squamous cell carcinomas are exposed to diffusion-limited hypoxia